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**MOUSE *Fkh<sup>sf</sup>* cDNA SEQUENCE**

1 GCTGATCCCC CTCTAGCAGT CCACTTCACC AAGGTGAGCG AGTGTCCCTG  
51 CTCTCCCCCA CCAGACACAG CTCTGCTGGC GAAAGTGGCA GAGAGGTATT  
101 GAGGGTGGGT GTCAGGAGCC CACCAGTACA GCTGGAAACA CCCAGCCACT  
151 CCAGCTCCCG GCAACTTCTC CTGACTCTGC CTTAGACGA GACTTGGAAG  
201 ACAGTCACAT CTCAGCAGCT CCTCTGCCGT TATCCAGCCT GCCTCTGACA  
251 AGAACCCAAT GCCCAACCCT AGGCCAGCCA AGCCTATGGC TCCTTCCTTG  
301 GCCCTTGCC CATCCCCAGG AGTCTTGCCA AGCTGGAAGA CTGCACCCAA  
351 GGGCTCAGAA CTTCTAGGGA CCAGGGGCTC TGGGGGACCC TTCCAAGGTC  
401 GGGACCTGCG AAGTGGGGCC CACACCTCTT CTTCTTGAA CCCCCTGCCA  
451 CCATCCCAGC TGCAGCTGCC TACAGTGCCC CTAGTCATGG TGGCACCGTC  
501 TGGGGCCCGA CTAGTCCCT CACCCACCT ACAGGCCCTT CTCCAGGACA  
551 GACCACACTT CATGCATCAG CTCTCCACTG TGGATGCCCA TGCCAGACC  
601 CCTGTGCTCC AAGTGCGTCC ACTGGACAAC CCAGCCATGA TCAGCCTCCC  
651 ACCACCTTCT GCTGCCACTG GGGTCTTCTC CCTCAAGGCC CGGCCTGGCC  
701 TGCCACCTGG GATCAATGTG GCCAGTCTGG AATGGGTGTC CAGGGAGCCA  
751 GCTCTACTCT GCACCTTCCC ACGCTCGGGT ACACCAGGA AAGACAGCAA  
801 CCTTTTGGCT GCACCCCAAG GATCCTACCC ACTGCTGGCA AATGGAGTCT  
851 GCAAGTGGCC TGGTTGTGAG AAGGTCTTCG AGGAGCCAGA AGAGTTTCTC  
901 AAGCACTGCC AAGCAGATCA TCTCCTGGAT GAGAAAGGCA AGGCCAGTG  
951 CCTCCTCCAG AGAGAAGTGG TGCAGTCTCT GGAGCAGCAG CTGGAGCTGG  
1001 AAAAGGAGAA GCTGGGAGCT ATGCAGGCCC ACCTGGCTGG GAAGATGGCG  
1051 CTGGCCAAGG CTCCATCTGT GGCCTCAATG GACAAGAGCT CTTGCTGCAT  
1101 CGTAGCCACC AGTACTCAGG GCAGTGTGCT CCCGGCCTGG TCTGCTCCTC

*Fig. 1A*



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1101 CGTAGCCACC AGTACTCAGG GCAGTGTGCT CCCGGCCTGG TCTGCTCCTC  
1151 GGGAGGCTCC AGACGGCGGC CTGTTTGCAG TCGGAGGCA CCTCTGGGGA  
1201 AGCCATGGCA ATAGTTCCTT CCCAGAGTTC TTCCACAACA TGGACTACTT  
1251 CAAGTACCAC AATATGCGAC CCCCTTTCAC CTATGCCACC CTTATCCGAT  
1301 GGGCCATCCT GGAAGCCCCG GAGAGGCAGA GGACACTCAA TGAAATCTAC  
1351 CATTGGTTTA CTCGCATGTT CGCCTACTTC AGAAACCACC CCGCCACCTG  
1401 GAAGAATGCC ATCCGCCACA ACCTGAGCCT GCACAAGTGC TTTGTGCGAG  
1451 TGGAGAGCGA GAAGGGAGCA GTGTGGACCG TAGATGAATT TGAGTTTCGC  
1501 AAGAAGAGGA GCCAACGCCC CAACAAGTGC TCCAATCCCT GCCCTTGACC  
1551 TCAAAACCAA GAAAAGGTGG GCGGGGGAGG GGGCCAAAAC CATGAGACTG  
1601 AGGCTGTGGG GGCAAGGAGG CAAGTCCTAC GTGTACCTAT GGAAACCGGG  
1651 CGATGATGTG CCTGCTATCA GGGCCTCTGC TCCCTATCTA GCTGCCCTCC  
1701 TAGATCATAT CATCTGCCTT ACAGCTGAGA GGGGTGCCAA TCCCAGCCTA  
1751 GCCCCTAGTT CCAACCTAGC CCCAAGATGA ACTTTCCAGT CAAAGAGCCC  
1801 TCACAACCAG CTATACATAT CTGCCTTGGC CACTGCCAAG CAGAAAGATG  
1851 ACAGACACCA TCCTAATATT TACTCAACCC AAACCCTAAA ACATGAAGAG  
1901 CCTGCCTTGG TACATTGCTG AACTTTCAA GTTAGTCATG CAGTCACACA  
1951 TGACTGCAGT CCTACTGACT CACACCCCAA AGCACTCACC CACAACATCT  
2001 GGAACCACGG GCACTATCAC ACATAGGTGT ATATACAGAC CCTTACACAG  
2051 CAACAGCACT GGAACCTTCA CAATTACATC CCCCCAACC ACACAGGCAT  
2101 AACTGATCAT ACGCAGCCTC AAGCAATGCC CAAAATACAA GTCAGACACA  
2151 GCTTGTCAGA

*Fig. 1B*

Title: IDENTIFICATION OF THE GENE CAUSING THE MOUSE SCURFY PHENOTYPE AND ITS HUMAN ORTHOLOG

Express Mail No. EV207743683US

Inventor(s): Mary E. Brunkow et al.

Serial No. 09/697,340

Docket No. 240083.501D4



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## MOUSE Fkh<sup>sf</sup> PROTEIN SEQUENCE

1 MPNPRPAKPM APSLALGPSP GVLPSWKTAP KGSELLGTRG SGGPFQGRDL  
51 RSGAHTSSSL NPLPPSQLQL PTVPLVMVAP SGARLGPSPH LQALLQDRPH  
101 FMHQLSTVDA HAQTPVLQVR PLDNPAMISL PPPSAATGVF SLKARPGGLPP  
151 GINVASLEWV SREPALLCTF PRSGTPRKDS NLLAAPQGSY PLLANGVCKW  
201 PGCEKVFEED EEFLKHCQAD HLLDEKGAQ CLLQREVVSQ LEQQLELEKE  
251 KLGAMQAHLA GKMLAKAPS VASMDKSSCC IVATSTQGSV LPAWSAPREA  
301 PDGGLFAVRR HLWGSNGNSS FPEFFHNMDY FKYHNMRRPF TYATLIRWAI  
351 LEAPERQRTL NEIYHWFTRM FAYFRNHPAT WKNAIRHNLS LHKCFVRVES  
401 EKGAVWTVDE FEFRRKRSQR PNKCSNPCP\*

*Fig. 2*



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HUMAN *FKH<sup>sf</sup>* cDNA Sequence

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1 GCACACACTC ATCGAAAAA ATTTGGATTA TTAGAAGAGA GAGGTCTGCG
51 GCTTCCACAC CGTACAGCGT GGTTTTTTCTT CTCGGTATAA AAGCAAAGTT
101 GTTTTTGATA CGTGACAGTT TCCCACAAGC CAGGCTGATC CTTTTCTGTC
151 AGTCCACTTC ACCAAGCCTG CCCTTGGACA AGGACCCGAT GCCCAACCCG
201 AGGCCTGGCA AGCCCTCGGC CCCTTCCTTG GCCCTTGGCC CATCCCCAGG
251 AGCCTCGCCC AGCTGGAGGG CTGCACCCAA AGCCTCAGAC CTGCTGGGGG
301 CCCGGGGCCC AGGGGAACC TTCCAGGGCC GAGATCTTCG AGGCGGGGCC
351 CATGCCTCCT CTTCTTCCTT GAACCCCATG CCACCATCGC AGCTGCAGCT
401 GCCCAGCTG CCCCTAGTCA TGGTGGCACC CTCGGGGGCA CGGCTGGGCC
451 CCTTGCCCCA CTTACAGGCA CTCCTCCAGG ACAGGCCACA TTTCATGCAC
501 CAGCTCTCAA CGGTGGATGC CCACGCCCCG ACCCCTGTGC TGCAGGTGCA
551 CCCCTGGAG AGCCAGCCA TGATCAGCCT CACACCACCC ACCACCGCCA
601 CTGGGGTCTT CTCCCTCAAG GCCCGGCCTG GCCTCCCACC TGGGATCAAC
651 GTGGCCAGCC TGAATGGGT GTCCAGGGAG CCGGCACTGC TCTGCACCTT
701 CCCAAATCCC AGTGACCCA GGAAGGACAG CACCCTTTCG GCTGTGCCCC
751 AGAGCTCCTA CCCACTGCTG GCAAATGGTG TCTGCAAGTG GCCCGGATGT
801 GAGAAGGTCT TCGAAGAGCC AGAGGACTTC CTCAAGCACT GCCAGGCGGA
851 CCATCTTCTG GATGAGAAGG GCAGGGCACA ATGTCTCCTC CAGAGAGAGA
901 TGGTACAGTC TCTGGAGCAG CAGCTGGTGC TGGAGAAGGA GAAGCTGAGT
951 GCCATGCAGG CCCACCTGGC TGGGAAAATG GCACTGACCA AGGCTTCATC
1001 TGTGGCATCA TCCGACAAGG GCTCCTGCTG CATCGTAGCT GCTGGCAGCC
1051 AAGGCCCTGT CGTCCAGCC TGGTCTGGCC CCCGGGAGGC CCCTGACAGC
1101 CTGTTTGCTG TCCGGAGGCA CCTGTGGGGT AGCCATGGAA ACAGCACATT
```

Fig. 3A

Title: IDENTIFICATION OF THE GENE CAUSING THE MOUSE SCURFY PHENOTYPE AND ITS HUMAN ORTHOLOG

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1151 CCCAGAGTTC CTCCACAACA TGGACTACTT CAAGTTCCAC AACATGCGAC  
1201 CCCCTTTTAC CTACGCCACG CTCATCCGCT GGGCCATCCT GGAGGCTCCA  
1251 GAGAAGCAGC GGACACTCAA TGAGATCTAC CACTGGTTCA CACGCATGTT  
1301 TGCCTTCTTC AGAAACCATC CTGCCACCTG GAAGAACGCC ATCCGCCACA  
1351 ACCTGAGTCT GCACAAGTGC TTTGTGCGGG TGGAGAGCGA GAAGGGGGCT  
1401 GTGTGGACCG TGGATGAGCT GGAGTTCCGC AAGAAACGGA GCCAGAGGCC  
1451 CAGCAGGTGT TCCAACCCTA CACCTGGCCC CTGACCTCAA GATCAAGGAA  
1501 AGGAGGATGG ACGAACAGGG GCCAAACTGG TGGGAGGCAG AGGTGGTGGG  
1551 GGCAGGGATG ATAGGCCCTG GATGTGCCCA CAGGGACCAA GAAGTGAGGT  
1601 TTCCACTGTC TTGCCTGCCA GGGCCCCTGT TCCCCGCTG GCAGCCACCC  
1651 CCTCCCCCAT CATATCCTTT GCCCAAGGC TGCTCAGAGG GGCCCCGGTC  
1701 CTGGCCCCAG CCCCCACCTC CGCCCCAGAC ACACCCCCCA GTCGAGCCCT  
1751 GCAGCCAAAC AGAGCCTTCA CAACCAGCCA CACAGAGCCT GCCTCAGCTG  
1801 CTCGCACAGA TTACTTCAGG GCTGGAAAAG TCACACAGAC ACACAAAATG  
1851 TCACAATCCT GTCCCTCAC

*Fig. 3B*

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## HUMAN FKHS<sup>sf</sup> PROTEIN SEQUENCE

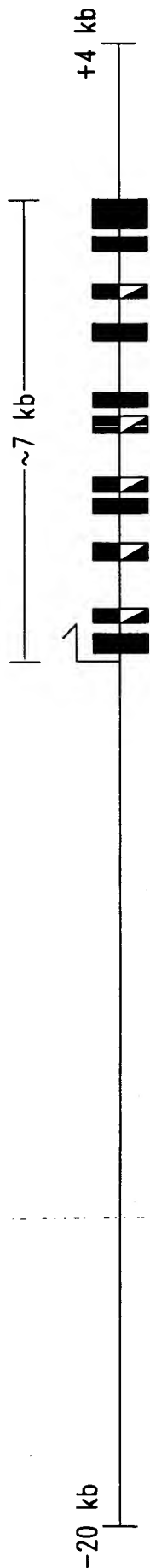
1 MPNPRPGKPS APSLALGPSP GASPSWRAAP KASDLLGARG PGGTFQGRDL  
51 RGGAHASSSS LNPMPPSQLQ LPTLPLVMVA PSGARLGPLP HLQALLQDRP  
101 HFMHQLSTVD AHARTPVLVQ HPLESPAMIS LTPPTTATGV FSLKARGLP  
151 PGINVASLEW VSREPALLCT FPNPSAPRKD STLSAVPQSS YPLLANGVCK  
201 WPGCEKVFEED PEDFLKHCQA DHLLDEKGRA QCLLQREMVQ SLEQQLVLEK  
251 EKLSAMQAHLE AGKMALTKAS SVASSDKGSC CIVAAGSQGP VVPAWSGPRE  
301 APDSLFAVRR HLWGSHGNST FPEFLHNMDY FKFHNMRPPF TYATLIRWAI  
351 LEAPEKQRTL NEIYHWFTRM FAFFRNHPAT WKNAIRHNLS LHKCFVRVES  
401 EKGAVWTVDE LEFRKKRSQR PSRCSNPTPG P\*

*Fig. 4*



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Vector for generation of FKH<sup>sf</sup> Transgenic mice



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Fig. 5

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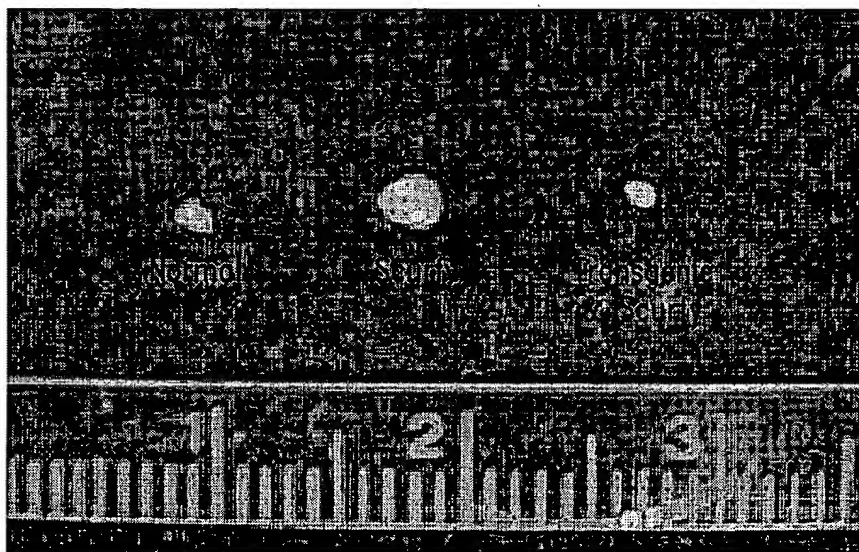
Docket No. 240083.501D4



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FKHsf Transgene corrects the defect in  
scurfy animals



*Fig. 6*





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FKHsf tg mice have reduce lymph node cells  
compared to normal cells

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Cell number	Mouse genotype		
	Normal	Scurfy	Transgenic
Cells / LN	0.92	1.97	0.29
Cells / Thymus	0.76	0.54	0.76

*Fig. 7*

FKHsf transgenic mice respond poorly to in vitro stimulation

Proliferation	Mouse genotype		
	Normal	Scurfy	Transgenic
No stimulation	778	23488	596
Anti-CD3+Anti-CD28	22932	225981	9106

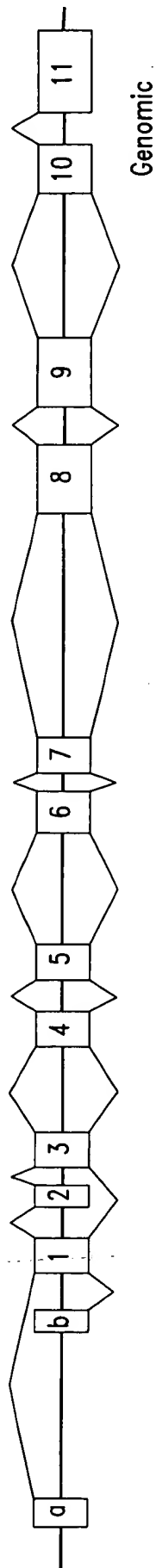
*Fig. 8*



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a 1 2 3 4 5 6 7 8 9 10 11

FKH<sup>sf</sup> cDNA



b 1 3 4 5 6 7 8 9 10 11

JM2 cDNA

**Comparison of FKH<sup>sf</sup> and JM2 cDNAs.** Exon/intron structure is shown (Genomic) as open rectangles (exons) joined by heavy horizontal lines (introns). Coding exons are numbered 1-11 as determined by sequence analysis of FKH<sup>sf</sup> cDNA; non-coding 5' exons are labelled *a* and *b*. The FKH<sup>sf</sup>-specific and JM2-specific splicing patterns and resulting cDNAs are indicated above and below the genomic structure, respectively.

*Fig. 9*

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Human FKH <sup>sf</sup>		Mouse Fkh <sup>sf</sup>	
N-terminal	ZNF	Mid	Forkhead
83.4%	95.8%	82.8%	96.4%

Human and mouse FKH<sup>sf</sup> proteins are highly conserved.

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*Fig. 10*